

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

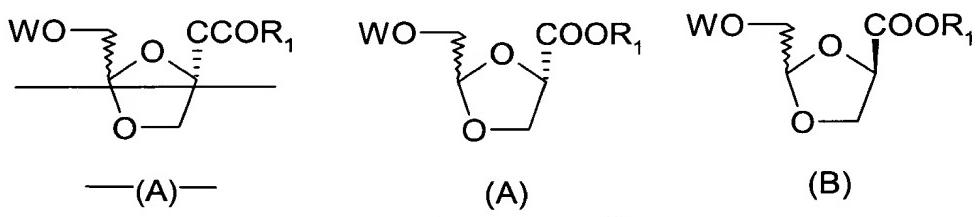
IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

The following listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Presently Amended): A process for stereoselectively producing a dioxolane nucleoside analogue from an anomeric mixture of β and α anomers represented by the following formula A or formula B:



wherein

W is benzyl or benzoyl, and

R₁ is selected from the group consisting of C₁₋₆ alkyl and C₆₋₁₅ aryl, wherein alkyl is a saturated or unsaturated, straight chain, branched chain or carbocyclic moiety, wherein the straight chain, branched chain or carbocyclic moiety is optionally interrupted by one or more heteroatoms selected from oxygen, nitrogen and sulfur, and said alkyl is unsubstituted or substituted by F, Cl, Br, I, hydroxyl, amino or C₆₋₂₀ aryl, and aryl is a carbocyclic moiety is optionally substituted and optionally interrupted by one heteroatom selected from oxygen, nitrogen and sulfur, and which contains at least one phenyl or naphthyl ring, the process comprising:

stereoselectively hydrolysing said mixture with an enzyme selected from the group consisting of cholesterol esterase, ESL-001-02, horse liver esterase, bovine pancreatic protease, α -chymotrypsin, protease from *Streptomyces caespitosus*, substilisin from *Bacillus licheniformis*, protease from *Aspergillus oryzae*, proteinase from *Bacillus licheniformis*, protease from *Streptomyces griseus*, acylase from *Aspergillus melleus*, proteinase from *Bacillus subtilis*, ESL-001-05, pronase protease from *Streptomyces griseus*, lipase from *Rhizopus arrhizus*, lipoprotein lipase from *Pseudomonas* species type B, lipase from *Pseudomonas cepacia* and bacterial proteinase, whereby said mixture is to stereoselectively

hydrolyse to predominantly one product anomer in which to form a product wherein R₁ is replaced with H, to form a product mixture;

separating the product anomer of the product mixture from unhydrolysed starting material of the product mixture; and

stereoselectively replacing the functional group COOR₁ at the C4 position (COOR₁) with a purinyl, or pyrimidinyl, an or analogue of purinyl or pyrimidinyl, or a derivative of purinyl or pyrimidinyl thereof to produce said dioxolane nucleoside analogue,

wherein said derivative refers to a purinyl or pyrimidinyl radical which is substituted by halogen, alkyl, aryl, cyano, carbamoyl, a primary, secondary or tertiary amino, hydroxyl or carbonyl, and

wherein said analogue refers to a purinyl or pyrimidinyl radical or a derivative of a purinyl or pyrimidinyl radical that is further modified by substituting one or more carbon in the ring structure with a nitrogen.

2. (Presently Amended): The process of claim 1, wherein the step of hydrolysing results in said the unhydrolysed starting material having an anomeric purity of at least 80%.

3. (Presently Amended): The process of claim 1, wherein the step of hydrolysing results in said the unhydrolysed starting material having an anomeric purity of at least 90%.

4. (Presently Amended): The process of claim 1, wherein the step of hydrolysing results in said the unhydrolysed starting material having an anomeric purity of at least 95%.

5. (Presently Amended): The process of claim 1, wherein the step of hydrolysing results in said the unhydrolysed starting material having an anomeric purity of at least 98%.

6. (Presently Amended): The process of claim 1, wherein the step of hydrolysing results in the said anomer product having an anomeric purity of at least 80%.

7. (Presently Amended): The process of claim 1, wherein the step of hydrolysing results in the said anomer product having an anomeric purity of at least 90%.

8. (Presently Amended): The process of claim 1, wherein the step of hydrolysing results in the said anomer product having an anomeric purity of at least 95%.

9. (Presently Amended): The process of claim 1, wherein the step of hydrolysing results in the said anomer product having an anomeric purity of at least 98%.

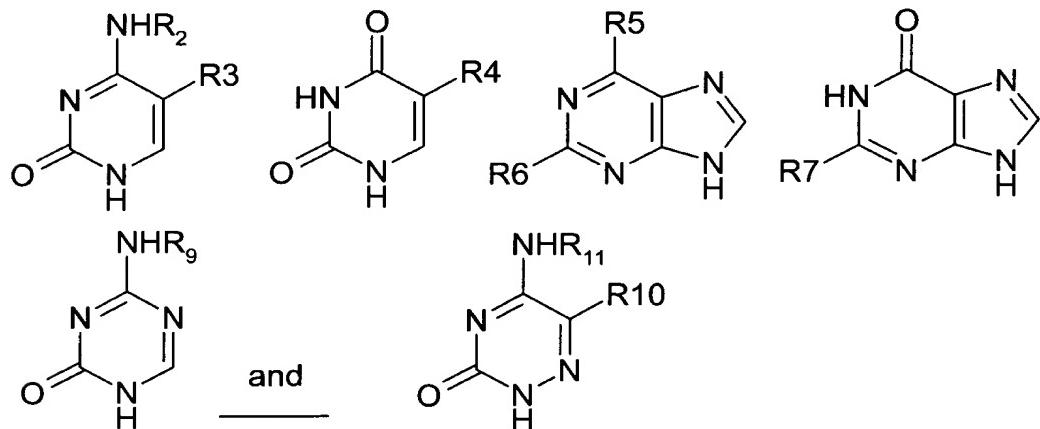
10. (Presently Amended): The process of claim 1, wherein W is benzyl and wherein the enzyme is selected from the group consisting of cholesterol esterase, ESL-001-02, horse liver esterase, bovine pancreatic protease, α -chymotrypsin, protease from *Streptomyces caespitosus*, subtilisin from *Bacillus licheniformis*.

11. (Original): The process of claim 10, wherein the enzyme is α -chymotrypsin.

12. (Original): The process of claim 10, wherein the enzyme is bovine pancreatic protease.

13. (Original): The process of claim 1, wherein W is benzoyl and wherein the enzyme is selected from the group consisting of protease from *Aspergillus oryzae*, proteinase from *Bacillus licheniformis*, subtilisin from *Bacillus licheniformis*, protease from *Streptomyces griseus*, acylase from *Aspergillus melleus*, proteinase from *Bacillus subtilis*, ESL-001-05, pronase protease from *Streptomyces griseus*, lipase from *Rhizopus arrhizus*, lipoprotein lipase from *Pseudomonas* species type B, bacterial proteinase, lipase from *Pseudomonas cepacia*.

14. (Presently Amended): The process of claim 1, wherein said purinyl, pyrimidinyl, an analogue of purinyl or pyrimidinyl, or a derivative of purinyl or pyrimidinyl ~~the purinyl or pyrimidinyl or analogue or derivative thereof is a radical selected from the group consisting of radicals of:~~



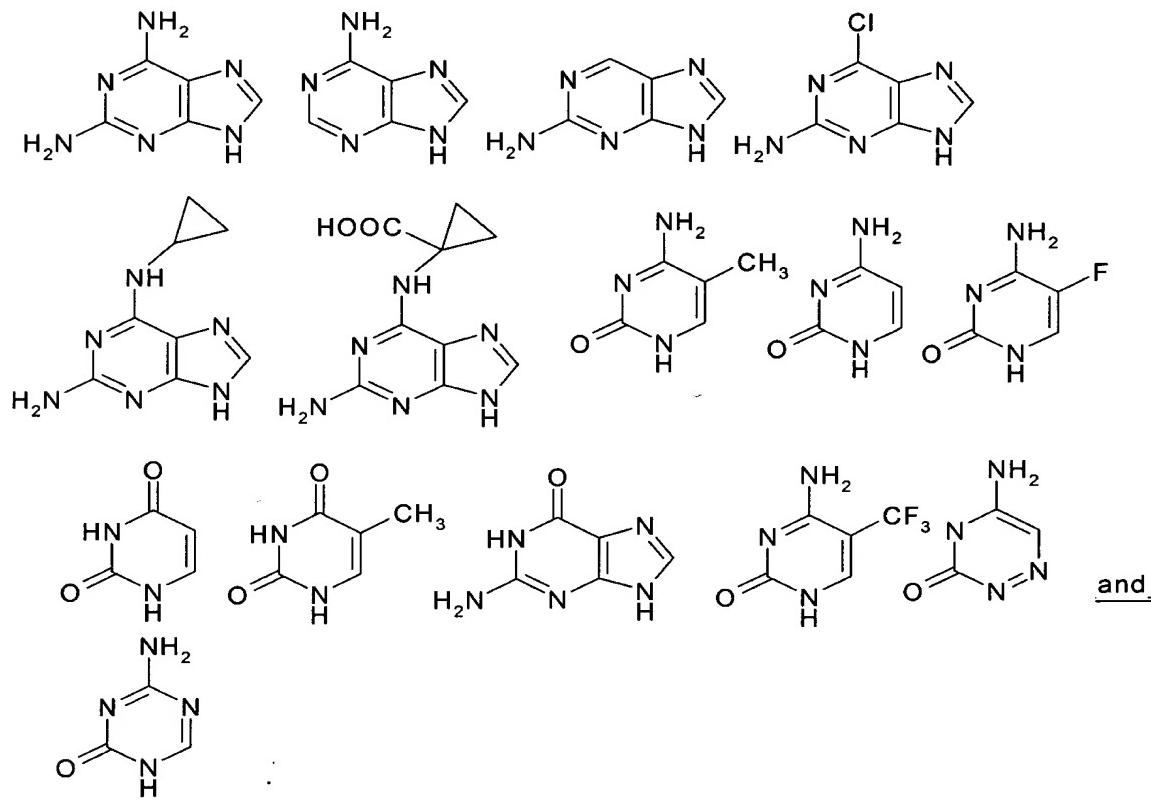
wherein

R₂, R₉ and R₁₁ are selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ acyl and R₈C(O) wherein R₈ is hydrogen or C₁₋₆ alkyl;

R₃, R₄ and R₁₀ are each independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, bromine, chlorine, fluorine, iodine and CF₃; and

R₅, R₆ and R₇ are each independently selected from the group consisting of hydrogen, bromine, chlorine, fluorine, iodine, amino, hydroxyl and C₃₋₆ cycloalkylamino.

15. (Presently Amended): The process of claim 1, wherein said purinyl, pyrimidinyl, an analogue of purinyl or pyrimidinyl, or a derivative of purinyl or pyrimidinyl ~~the purine or pyrimidine base or analogue or derivative thereof~~ is a radical selected from the group consisting of radicals of:



16. (Presently Amended): The process of claim 1, wherein the step of replacing further comprises:

acylating the separated anomer product the second mixture to produce an acylated second mixture; and

glycosylating the acetylated separated anomer product second mixture with said purinyl, pyrimidinyl, an analogue of purinyl or pyrimidinyl, or a derivative of purinyl or pyrimidinyl, ~~the purine or pyrimidine base or analogue or derivative thereof~~ and a Lewis Acid to produce said the dioxolane nucleoside analogue.

17. (New): A process according to claim 10, wherein said enzyme is cholesterol

esterase.

18. (New): A process according to claim 10, wherein said enzyme is ESL-001-02.
19. (New): A process according to claim 10, wherein said enzyme is horse liver esterase.
20. (New): A process according to claim 10, wherein said enzyme is protease from *Streptomyces caespitosus*.
21. (New): A process according to claim 10, wherein said enzyme is substilisin from *Bacillus licheniformis*.
22. (New): A process according to claim 13, wherein said enzyme is protease from *Aspergillus oryzae*.
23. (New): A process according to claim 13, wherein said enzyme is proteinase from *Bacillus licheniformis*.
24. (New): A process according to claim 13, wherein said enzyme is subtilisin from *Bacillus licheniformis*.
25. (New): A process according to claim 13, wherein said enzyme is protease from *Streptomyces griseus*.
26. (New): A process according to claim 13, wherein said enzyme is acylase from *Aspergillus melleus*.
27. (New): A process according to claim 13, wherein said enzyme is proteinase from *Bacillus subtilis*.

28. (New): A process according to claim 13, wherein said enzyme is ESL-001-05.

29. (New): A process according to claim 13, wherein said enzyme is pronase protease from *Streptomyces griseus*.

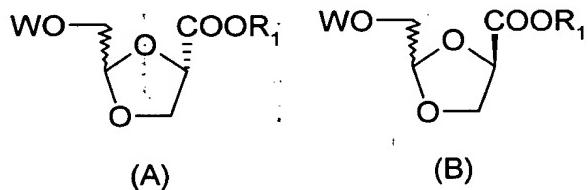
30. (New): A process according to claim 13, wherein said enzyme is lipase from *Rhizopus arrhizus*.

31. (New): A process according to claim 13, wherein said enzyme is lipoprotein lipase from *Pseudomonas* species type B.

32. (New): A process according to claim 13, wherein said enzyme is bacterial proteinase.

33. (New): A process according to claim 13, wherein said enzyme is lipase from *Pseudomonas cepacia*.

34. (New): A process for stereoselectively producing a dioxolane nucleoside analogue from an anomeric mixture of β and α anomers represented by the following formula A or formula B:



wherein

W is benzyl or benzoyl, and

R₁ is selected from the group consisting of C₁₋₆ alkyl which is straight chain or branched chain and which is unsubstituted or substituted by F, Cl, Br, I, hydroxyl, amino or C₆₋₂₀ aryl, C₃₋₆ cycloalkyl which is unsubstituted or by C₁₋₆ alkyl, F, Cl, Br, I, amino or NO₂.

and C₆₋₁₅ aryl, said process comprising:

stereoselectively hydrolysing said mixture with an enzyme, wherein

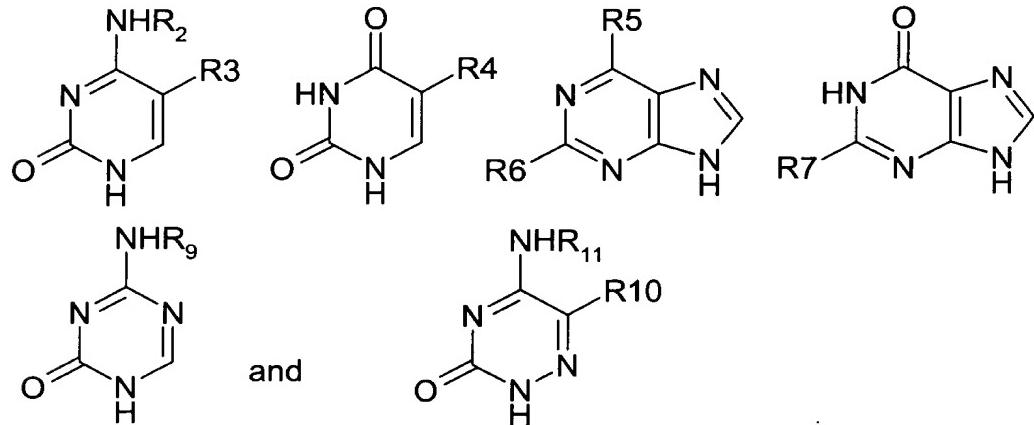
when W is benzyl said enzyme is selected from the group consisting of cholesterol esterase, ESL-001-02, horse liver esterase, bovine pancreatic protease, α -chymotrypsin, protease from *Streptomyces caespitosus*, substilisin from *Bacillus licheniformis*, and

when W is benzoyl said enzyme is selected from the group consisting of protease from *Aspergillus oryzae*, proteinase from *Bacillus licheniformis*, subtilisin from *Bacillus licheniformis*, protease from *Streptomyces griseus*, acylase from *Aspergillus melleus*, proteinase from *Bacillus subtilis*, ESL-001-05, pronase protease from *Streptomyces griseus*, lipase from *Rhizopus arrhizus*, lipoprotein lipase from *Pseudomonas* species type B, bacterial proteinase, lipase from *Pseudomonas cepacia*,

whereby said mixture is stereoselectively hydrolysed to predominantly one product anomer in which R₁ is replaced with H, to form a product mixture;

separating the product anomer of the product mixture from unhydrolysed starting material of the product mixture; and

stereoselectively replacing the functional group COOR₁ at the C4 position with a radical selected from the group consisting of radicals of:



wherein

R₂, R₉ and R₁₁ are selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ acyl and R₈C(O) wherein R₈ is hydrogen or C₁₋₆ alkyl;

R_3 , R_4 and R_{10} are each independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, bromine, chlorine, fluorine, iodine and CF₃; and

R_5 , R_6 and R_7 are each independently selected from the group consisting of hydrogen, bromine, chlorine, fluorine, iodine, amino, hydroxyl and C₃₋₆ cycloalkylamino,

to thereby produce said dioxolane nucleoside analogue.

35. (New): A process according to claim 34, wherein said enzyme is cholesterol esterase.

36. (New): A process according to claim 34, wherein said enzyme is ESL-001-02.

37. (New): A process according to claim 34, wherein said enzyme is horse liver esterase.

38. (New): A process according to claim 34, wherein said enzyme is protease from *Streptomyces caespitosus*.

39. (New): A process according to claim 34, wherein said enzyme is substilisin from *Bacillus licheniformis*.

40. (New): A process according to claim 34, wherein said enzyme is protease from *Aspergillus oryzae*.

41. (New): A process according to claim 34, wherein said enzyme is proteinase from *Bacillus licheniformis*.

42. (New): A process according to claim 34, wherein said enzyme is protease from *Streptomyces griseus*.

43. (New): A process according to claim 34, wherein said enzyme is acylase from

Aspergillus melleus.

44. (New): A process according to claim 34, wherein said enzyme is proteinase from *Bacillus subtilis*.

45. (New): A process according to claim 34, wherein said enzyme is ESL-001-05.

46. (New): A process according to claim 34, wherein said enzyme is pronase protease from *Streptomyces griseus*.

47. (New): A process according to claim 34, wherein said enzyme is lipase from *Rhizopus arrhizus*.

48. (New): A process according to claim 34, wherein said enzyme is lipoprotein lipase from *Pseudomonas* species type B.

49. (New): A process according to claim 34, wherein said enzyme is bacterial proteinase.

50. (New): A process according to claim 34, wherein said enzyme is lipase from *Pseudomonas cepacia*.